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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,301	12/16/2004	Ganapathy Gopalrathnam	X-15199	3398

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EXAMINER	
BARNHART, LORA ELIZABETH	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/506,301	GOPALRATHNAM ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *20-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment received 8/15/05 in which claim 9 is amended is noted. Claims 1-24 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-8, in the reply filed on 8/15/05 is acknowledged. The traversal is on the ground(s) that the inventive groups share a special technical feature, namely a pharmaceutical composition comprising activated protein C and a chelating agent. Applicant alleges that Foster et al. does not teach or suggest a pharmaceutical composition comprising activated protein C and a chelating agent and, therefore, said composition is not known in the art. This argument has been fully considered, but it is not persuasive.

Group II, claims 9-19, and Group VII, claim 24, are rejoined to Group I in light of the claim amendments.

Patents are relevant as prior art for all they contain. "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See M.P.E.P. §2123. By applicant's own admission (Remarks, page 6), Foster et al. suggest pharmaceutical compositions

comprising activated protein C and EDTA (column 9, line 62, through column 10, line 5). The fact that Foster et al. do not exemplify pharmaceutical compositions does not mean that such compositions were not contemplated; indeed, they clearly were contemplated.

The expression "special technical feature" refers to those features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Thus, a feature found in the prior art, such as a pharmaceutical composition comprising activated protein C and a chelator, cannot be considered to be a special technical feature.

Even if pharmaceutical compositions comprising activated protein C and a chelator constituted a special technical feature (which the examiner does not concede), the methods of production in Groups III and IV lack inventive unity with the product of Group I, because the methods of Groups III and IV do not result in the product of Group I **as claimed**. Similarly, the methods of Groups V and VI do not require the use of the product of Group I **as claimed**. The methods of Groups III-VI are drawn to the production and use of lyophilized compositions, and the product of Group I is not necessarily lyophilized.

Applicant's election with traverse of various species in the same reply is acknowledged. The traversal is on the ground(s) that the species behave similarly in the context of the claimed invention. This argument is persuasive. The requirement for an election of species is withdrawn.

The requirement is still deemed proper and is therefore made FINAL. Claims 20-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being

drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/15/05. Examination will continue on claims 1-19 and 24 ONLY.

Claim Objections

Claims 2 and 9 are objected to for informalities. Correction is requested.

Claim 2 is does not end with a period.

A space has been omitted between "Claim" and "1" at line 2 of claim 9.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is confusing in that it depends from claim 9, which is not drawn to a lyophilized composition, but requires the diluent to be a "reconstitution diluent." According to the definition in the specification, a reconstitution diluent is specifically used in conjunction with lyophilized compositions (page 4, lines 15-16. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Carlson et al. (2000, U.S. Patent 6,159,468; IDS reference AU). The claims are drawn to a pharmaceutical composition comprising activated protein C and a chelating agent. In some dependent claims, the composition is lyophilized; further comprises a bulking agent, which may be selected from a list; further comprises a buffer selected from a list, which may provide a specific pH; further comprises a salt, which may be selected from a list; or further comprises a diluent, which may have particular properties.

Carlson et al. teach a composition comprising human protein C, 0.4M sodium chloride, and 20mM Tris-acetate, pH 6.5 (Preparation 1); Preparation 1 is made 5mM in EDTA and passed over a thrombin column, thus activating protein C, and eluted with Tris buffer and lyophilized (Preparation 2). Preparation 2 therefore comprises activated protein C, EDTA (a chelator; see column 7, lines 1-2), Tris-acetate, and sodium chloride at pH 6.5 (column 7, lines 26-27; Example 1). Carlson et al. further teach dissolving lyophilized Preparation 2 in phosphate buffer, then adding a bulking agent (either mannitol, sucrose, trehalose, or raffinose) and re-lyophilizing (Examples 1 and 2).

Claims 1, 9, and 11-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Foster et al. (1996, U.S. Patent 5,516,650; IDS reference AO) taken in light of Carlson et al. (AU). The claim is drawn to a pharmaceutical composition comprising activated protein C and a chelating agent. In some claims, the composition further comprises a diluent.

Foster et al. teach a solution comprising activated protein C, EDTA (a chelating agent), and TBS (Tris-buffered saline) in water (column 21, lines 20-24). Carlson et al. is cited as evidence that Tris is a pharmaceutically acceptable buffer (column 3, lines 9-12).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-19 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carlson et al. (2000, U.S. Patent 6,159,468; IDS reference AU). The claims are drawn to a pharmaceutical composition comprising activated protein C and a chelating agent. In some dependent claims, the composition is lyophilized; further comprises a bulking agent, which may be selected from a list; further comprises a buffer selected from a list, which may provide a specific pH; further comprises a salt, which may be selected from a list; or further comprises a diluent, which may have particular properties.

As discussed above, Carlson et al. teach a composition comprising human protein C, 0.4M sodium chloride, and 20mM Tris-acetate, pH 6.5 (Preparation 1); Preparation 1 is made 5mM in EDTA and passed over a thrombin column, thus activating protein C, and eluted with Tris buffer and lyophilized (Preparation 2). Preparation 2 therefore comprises activated protein C, EDTA (a chelator; see column 7, lines 1-2), Tris-acetate, and sodium chloride at pH 6.5 (column 7, lines 26-27; Example 1). Carlson et al. further teach dissolving lyophilized Preparation 2 in phosphate buffer, then adding a bulking agent (either mannitol, sucrose, trehalose, or raffinose) and re-lyophilizing (Examples 1 and 2). Carlson et al. do not exemplify other buffers or salts.

Carlson et al. teach that mannitol, trehalose, raffinose, and sucrose are all acceptable bulking agents for the composition (column 3, lines 29-30 and 60-63). Carlson et al. further teach that Tris buffers, citrate buffers, phosphate buffers, and acetate buffers are all pharmaceutically acceptable buffers (column 3, lines 9-12, and

column 4, lines 20-27). Carlson et al. teach that the pH of the composition, upon reconstitution, is between 5.5 and 6.5 (column 3, lines 30-33). Carlson et al. further teach that potassium chloride and sodium chloride are acceptable salts for inclusion in the composition (column 4, lines 37-41). Carlson et al. teach the importance of removal of residual calcium using chelators, for example EDTA, from protein C preparations (column 6, lines 35-50). Finally, Carlson et al. contemplate the administration of the composition to a patient in need thereof (column 5, lines 38-58).

The selection of bulking agent, salt, and buffer from among the recited species clearly would have been a routine matter of optimization on the part of the artisan of ordinary skill, said artisan recognizing that Carlson et al. teach that said species are acceptable substitutes for each other (see above). A holding of obviousness over the cited claims is therefore clearly required.

While the composition of Carlson et al. comprises some EDTA from the activation step (column 7, lines 1-3), a person of ordinary skill in the art would have had a reasonable expectation of success in including additional EDTA in the composition of Carlson et al. because EDTA is taught by Carlson et al. not to affect the composition's essential properties. The skilled artisan would have been motivated to include additional EDTA for the expected benefit that activated protein C would be protected from calcium and other divalent ions. It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to include additional EDTA in the composition of Carlson et al. because Carlson et al. suggest its inclusion to chelate metal ions.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Friday, 8:00am - 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SANDRA E. SAUCIER
PRIMARY EXAMINER

Lora E Barnhart